

Applicants: Hermona Soreq et al.
Serial No.: 09/310,638
Filed : May 12, 1999
Page 3

In the claims:

Please amend the pending claims under the provisions of revised 37 C.F.R. §1.121 as follows.

- 1. (withdrawn) A substantially pure DNA sequence encoding acetylcholinesterase (AChE) selected from the group consisting of:
 - (a) genomic clones having a nucleotide sequence derived from the genomic region of a human AChE gene;
 - (b) cDNA clones having a nucleotide sequence derived from the sequence of said genomic clones of (a);
 - (c) DNA sequences capable of hybridization to the clones of (a) and (b) under moderately stringent conditions and which encode biologically active AChE; and
 - (d) DNA sequences which are degenerate as a result of the genetic code to the DNA sequences defined in (a), (b) and (c) and which encode biologically active AChE for use in biopharming.--

- 2. (withdrawn) A DNA sequence according to claim 1, wherein said sequence encodes human AChE or biologically active derivatives thereof.--

- 3. (withdrawn) A DNA sequence according to claim 2, which has all or part of the nucleotide sequence substantially as depicted in Fig. 1A, (SEQ ID NO:1) and which encodes an amino acid sequence substantially similar or identical to all or part of the sequence of amino acid residues depicted in Fig. 1B (SEQ ID NO:2).--

Applicants: Hermona Soreq et al.
Serial No.: 09/310,638
Filed : May 12, 1999
Page 4

- 4. (withdrawn) A DNA sequence according to claim 2, which has all or part of the nucleotide (SEQ ID NO:3) sequences substantially as depicted in Fig. 1C, and which encodes an amino acid sequence substantially similar or identical to all or part of the sequence of amino acid residues (SEQ ID NO:4) also depicted in Fig. 1C.--
- 5. (withdrawn) A DNA sequence according to claim 2, which has all or part of the nucleotide sequence (SEQ ID NO:5) substantially as depicted in Fig. 1D, and which encodes an amino acid sequence (SEQ ID NO:6) substantially similar or identical to all or part of the sequence of amino acid residues also depicted in Fig. 1D.--
- 6. (withdrawn) A recombinant expression vector comprising a DNA sequence according to claim 1.--
- 7. (withdrawn) A recombinant expression vector for use in biopharming, according to claim 6 which has a DNA sequence encoding a human AChE or biologically active derivatives thereof selected from:
 - (a) a DNA sequence which has all or part of the nucleotide sequence (SEQ ID NO:1) substantially as depicted in Fig. 1A, and which encodes an amino acid sequence substantially similar or identical to all or part of the sequence of amino acid residues (SEQ ID NO:2) depicted in Fig. 1B.
 - (b) a DNA sequence which has all or part of the nucleotide sequences substantially as depicted in Fig. 1C, and which encodes an amino acid sequence substantially similar or identical to all or part of

Applicants: Hermona Soreq et al.
Serial No.: 09/310,638
Filed : May 12, 1999
Page 5

the sequence of amino acid residues (SEQ ID NO:3) also depicted in Fig. 1C.

(c) a DNA sequence which has all or part of the nucleotide sequence (SEQ ID NO:5) substantially as depicted in Fig. 1D, and which encodes an amino acid sequence substantially similar or identical to all or part of the sequence of amino acid residues (SEQ ID NO:6) also depicted in Fig. 1D.--

--8. (withdrawn) A recombinant expression vector according to claim 7, which has a promoter controlling the transcription of said sequence encoding AChE selected from the group of eukaryotic host cell compatible promoters consisting of CMV, CMV-like, AChE and AChE-like promoters.--

--9. (withdrawn) A eukaryotic host cell transformed with the expression vector according to claim 6, said host cell being capable of expressing AChE when cultured under conditions promoting AChE expression.--

--10. (withdrawn) A eukaryotic host cell transformed with the expression vector according to claim 7, said host cell being capable of expressing AChE when cultured under conditions promoting AChE expression.--

--11. (currently amended) A transgenic non-human animal comprising a recombinant nucleic acid expression vector encoding a heterologous cholinesterase (ChE) enzyme selected from the group consisting of:

- (a) wild-type human AChE;
- (b) wild-type human BChE;

Applicants: Hermona Soreq et al.
Serial No.: 09/310,638
Filed : May 12, 1999
Page 6

- (c) biologically active variants of the AChE and BChE of (a) and (b); and
- (d) wild-type insect ChEs, wherein the nucleic acid is expressed in the germ cells and somatic cells of the transgenic animal at a higher level relative to a nontransgenic animal.--

--12. (previously presented) The transgenic non-human animal of claim 11, wherein the animal is *Xenopus* or mammal.--

--13. (previously presented) The transgenic non-human animal of claim 12, wherein the recombinant expression vector comprises a nucleic acid encoding a human AChE or a biologically active derivative thereof, which nucleic acid comprises:

- (a) consecutive nucleotides having the nucleic acid sequence set forth in SEQ ID NO: 1 or a fragment thereof;
- (b) consecutive nucleotides having the nucleic acid sequence set forth in SEQ ID NO: 3 or a fragment thereof; or
- (c) consecutive nucleotides having the nucleic acid sequence set forth in SEQ ID NO:5 or a fragment thereof.--

--14. (previously presented) The transgenic non-human animal of claim 11, wherein the recombinant expression vector comprises a promoter which controls the transcription of the nucleic acid sequence encoding AChE and is selected from the group of eukaryotic host cell compatible promoters.--

Applicants: Hermona Soreq et al.
Serial No.: 09/310,638
Filed : May 12, 1999
Page 7

- 15. (withdrawn) Acetylcholinesterase produced by a eukaryotic host cell according to claim 9.--
- 16. (withdrawn) Acetylcholinesterase produced by a eukaryotic host cell according to claim 10.--
- 17. (currently amended) A transgenic non-human animal [assay system for studying secretion, control of production and biochemical properties of cholinesterases in mammalian milk,] capable of expressing detectable amounts of cholinesterase enzyme in its mammary glands comprising the transgenic mammal of claim 12, wherein the transgenic mammal is female and the expression vector further comprises a promoter operably linked to the nucleic acid encoding the heterologous cholinesterase enzyme which (i) is selected from the group of eukaryotic host cell compatible promoters and (ii) directs and controls expression of the nucleic acid encoding cholinesterase enzyme in mammary glands of the transgenic mammal.--
- 18. (currently cancelled)
- 19. (currently amended) The transgenic non-human mammal of claim [[18]] 17, wherein the ChE enzyme is wild-type human AChE or a biologically active variant thereof.--
- 20. (previously presented) The transgenic non-human mammal of claim 19, wherein the AChE variant is selected from the group consisting essentially of recombinantly-produced point mutation and deletion of one or more residues and mutations.--

Applicants: Hermona Soreq et al.
Serial No.: 09/310,638
Filed : May 12, 1999
Page 8

- 21. (withdrawn) A method of treatment of acute traumatic injury by administering to a patient in need of such treatment a therapeutically effective amount of at least one of an antisense oligodeoxynucleotide selected from the group consisting essentially of Seq. ID. No. 1-6.--
- 22. (withdrawn) The method according to claim 21, wherein said administration step further results in preventing AChE overproduction and excessive dendritic growth.--
- 23. (currently amended) The transgenic non-human mammal of claim 12, wherein the mammal is female and the ChE enzyme expressed in the cells of the mammal is wild-type human AChE or a biologically active variant thereof.--
- 24. (currently amended) A method of producing recombinant [[human AChE]] cholinesterase enzyme comprising the steps of:
- (i) providing [[a]] the lactating transgenic non-human female mammal according to claim [[23]] 17;
 - (ii) obtaining milk from the transgenic non-human mammal of step (i); and
 - (iii) isolating human AChE from the milk obtained in step (ii),
- so as to thereby produce recombinant human AChE.--
- 25. (previously cancelled)
- 26. (currently amended) The transgenic non-human animal of claim 12, wherein the mammal is a mouse, a goat, a cow or a pig.--

Applicants: Hermona Soreq et al.
Serial No.: 09/310,638
Filed : May 12, 1999
Page 9

--27. (new) A transgenic non-human animal assay system for studying secretion, control of production and biochemical properties of cholinesterases in mammalian milk comprising the transgenic mammal of claim 17.--